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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/865,198	05/24/2001	Zhenping Zhu	11245/47102	3886

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	8

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/865,198	ZHU, ZHENPING	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *One* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-77* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Fax cover sheet* .

DETAILED ACTION

1. The location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1644, Group 1640, Technology Center 1600.

2. **Please Note**: In an effort to enhance communication with our customers and reduce processing time, Group 1640 is running a Fax Response Pilot for Written Restriction Requirements. A dedicated Fax machine is in place to receive your responses. The Fax number is 703-308-4315. A Fax cover sheet is attached to this Office Action for your convenience. We encourage your participation in this Pilot program. If you have any questions or suggestions please contact Paula Hutzell, Ph.D., Supervisory Patent Examiner at Paula.Hutzell@uspto.gov or 703-308-4310. Thank you in advance for allowing us to enhance our customer service. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

3. Claims 1-77 are pending.

Election/Restrictions

4. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-3, 5, 7-24, 25, 26, 27, 36, 39-48, and 50-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** and wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for FLT1,** at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

II. Claims 1-3, 5, 7-24, 26, 28, 37, 39-48, 50-52 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for FLT4**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

III. Claims 1-3, 5, 7-24, 26, 29, 33, 37, 39-48, 50-52 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for EGF-R**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

IV. Claims 1-3, 5, 7-24, 26, 30, 33, 37, 39-48, 50-52 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have

different specificities wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for HER-2**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

V. Claims 1-3, 5, 7-24, 26, 31, 33, 37, 39-48, 50-52 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for FGF-R**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

VI. Claims 1-3, 5, 7-24, 26, 32-33, 37, 39-48, 50-52 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for PDGF-R**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

VII. Claims 1-3, 5, 7-24, 26, 34, 37, 39-48, 50-52 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable

association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is a specific **VEGF receptor KDR and the other antigen-binding site is specific for Tek**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

VIII. Claims 1-3, 5, 7-24, 26, 35, 37, 39-48, 50-52 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for Tie**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

IX. Claims 1-3, 5, 7-21, 29-30, 38, 39-48, 50-52 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **EGF-R and the other antigen-binding site is specific for HER2**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

X. Claims 1-2, 4, 6, 7-25, 27, 39-47, 49, 53-54 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **VEGF receptor encoded by the FLT1 gene**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XI. Claims 1-2, 4, 6, 7-25, 39-47, 49 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **VEGF receptor encoded by the FLK1 gene**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XII. Claims 1-2, 4, 6, 7-24, 26, 39-47, 49-52 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have

same specificities, and wherein at least one of the antigen binding sites is specific for **VEGF receptor KDR**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XIII. Claims 1-2, 4, 6, 7-24, 28, 39-47, 49 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **VEGF receptor FLT4**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XIV. Claims 1-2, 4, 6, 7-21, 29, 33, 39-47, 49 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **EGF receptor**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XV. Claims 1-2, 4, 6, 7-21, 30, 33, 39-47, 49 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-

association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **Tyrosine kinase receptor HER2**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XVI. Claims 1-2, 4, 6, 7-21, 31, 33, 39-47, 49 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **FGF receptor**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XVII. Claims 1-2, 4, 6, 7-21, 32, 33, 39-47, 49 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **PDGF receptor**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XVIII. Claims 1-2, 4, 6, 7-21, 33-34, 39-47, 49 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1

domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **Tek**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XIX. Claims 1-2, 4, 6, 7-21, 35, 39-47, 49 and 55-62, drawn to an antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **Tie-2**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XX. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** and wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for FLT1,** at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXI. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable

association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for FLT4**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXII. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for EGF-R**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXIII. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for HER-2**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXIV. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for FGF-R**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXV. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for PDGF-R**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXVI. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have

different specificities wherein one of the antigen binding sites is a specific **VEGF receptor KDR and the other antigen-binding site is specific for Tek**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXVII. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **VEGF receptor KDR and the other antigen-binding site is specific for Tie**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXVIII. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **different specificities** wherein one of the antigen binding sites is specific for **EGF-R and the other antigen-binding site is specific for HER2**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXIX. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable

association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **VEGF receptor encoded by the FLT1 gene**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXX. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **VEGF receptor encoded by the FLK1 gene**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXXI. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **VEGF receptor KDR**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXXII. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **VEGF receptor FLT4**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXXIII. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **EGF receptor**, at least one of the antigen binding is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXXIV. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for

Tyrosine kinase receptor HER2, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXXV. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **FGF receptor**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXXVI. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **PDGF receptor**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXXVII. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have

same specificities, and wherein at least one of the antigen binding sites is specific for **Tek**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

XXXVIII. Claims 64-68, drawn to a method of making a specific antigen-binding protein comprising a complex of two first polypeptides and two second polypeptides, said first polypeptide having an antigen-binding site located to the N terminus of an immunoglobulin light chain constant domain said C_L domain capable of stable association with an Ig heavy chain first domain (C_H1 domain), and said second polypeptide having an antigen-binding site located to the N terminus of said CH-1 domain followed by one or more heavy chain constant domains capable of stable self-association wherein the antigen-binding sites of said first and second polypeptides have **same specificities**, and wherein at least one of the antigen binding sites is specific for **Tie-2**, at least one of the antigen binding sites is specific for a cell surface receptor or a cytokine receptor, classified in Class 424, subclass 136.1.

IXL. Claims 69-71, drawn to a method of neutralizing the activation of a VEGF receptor which comprises treating a cell with an antigen-binding protein wherein the at least one of the antigen-binding sites is specific for KDR and at least one of the antigen-binding sites is specific for FLT1, classified in class 435, subclass 7.21.

XL. Claims 72-74, drawn to a method of reducing tumor growth which comprises treating a cell with a specific binding protein wherein at least one of the antigen-binding sites is specific for KDR and at least one of the antigen-binding sites is specific FLT1, classified in Class 424, subclass 134.1.

XLI. Claims 75-77, drawn to a method of inhibiting angiogenesis which comprises treating a cell with a specific antigen-binding protein wherein at least one of the antigen-binding sites is specific for KDR and at least one of the antigen-binding sites is specific FLT1, classified in Class 424, subclass 134.1.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Groups I-XIX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the

products as claimed differ with respect to structure and physiochemical properties and binding specificity. Therefore, they are patentably distinct.

Inventions of Groups XX-XLI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the methods of making different products versus the method of neutralizing the activation of a VEGF receptor or inhibiting tumor growth with different products differ with their respect to their process steps and endpoints. Therefore, they are patentably distinct.

Inventions of Groups (I-XIX) and Groups (XX-XLI) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the products as claimed can be used in materially different process such as screening assays. Therefore, they are patentably distinct.

5. Because these inventions are distinct for the reasons given above and the searches are not co-extensive, restriction for examination purposes as indicated is proper.

6. Irrespective of whichever group the applicant may elect, the applicant is further required under 35 U.S.C. 121 to elect:

A) If Group I, II, III, IV, V, VI, VII, VIII, IX, X, XI, XII, XIII, XIV, XV, XVI, XVII, XVIII or XIX is elected, the Applicant is required to elect an antigen-binding protein comprising (1) **one specific cell-surface antigen** wherein the cell surface antigen is a **receptor** such as the ones recited in claim 46 or (2) **one specific cell-surface antigen** wherein the cell-surface antigen is a **cytokine or lymphokine** such as the ones recited in claims 43. These cell-surface antigen such as the ones recited in claims 43 and 46 are patentably distinct because the cell-surface antigen receptors differ with respect to their structures, and binding specificity, and the cell-surface cytokines differ with respect their structures, physiochemical properties and mode of action. Therefore, they are patentably distinct.

B) If Group XX, XXI, XXII, XXIII, XXIV, XXV, XXVI, XXVII, XXVIII, XXIX, XXX, XXXI, XXXII, XXXIII, XXXIV, XXXV, XXXVI, XXXVII is elected, the Applicant is required to elect

a method of making an antigen-binding protein which comprises at least one of the antigen binding site is specific for a cell-surface antigen of an immune system effector cell wherein the cell-surface antigen is (1) **one specific cell-surface receptor** such as the ones recited in claim 46 or (2) **one specific cytokine or lymphokine** such as the ones recited in claims 43. These cell-surface antigen such as the ones recited in claims 43 and 46 are patentably distinct because the cell-surface antigen receptors differ with respect to their structures, and binding specificity, and the cell-surface cytokines differ with respect their structures, physiochemical properties and mode of action. Therefore, they are patentably distinct.

7. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1 and 42 are generic.

8. Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

9. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. M.P.E.P. § 809.02(a).

10. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

11. Due to the complexity of the claimed invention an oral restriction was not made.

12. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
July 1, 2002

Christina Chan

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